

July 18, 1947.

Dear Newcombe-

Thanks for the information in your letter just received.

I wish it were possible for me to visit the CSH lab. again, but I just don't see how I can manage it. My wife and I are leaving for Woods Hole on the first of August for a vacation, and to write. Meanwhile, I have a lot of things to clean up here, and I just can't find the time. Could I simply reverse your invitation?

From the tone of your letter more than anything else I gather that you are strongly impressed with the possibility that irradiation, in addition to inducing changes at the V_1 locus to a resistant allele, may also induce mutations to alleles which although sensitive are characterized by high(er) rates of mutation to a resistant state. I must say that I have been led to the same notions on ~~general~~ general considerations, as well as by my studies on stable and unstable Lac- mutants. On the basis of the efficacy of radiation in inducing reverse-mutation in *Drosophila*, Muller was led to the conclusion that absorbed energy could somehow be "canalized" to the critical part of the gene that must be restored. My wife has been working on induced reversions in *Neurospora*, and I think that it would be unwise to categorize any reversion necessarily as a precise restoration of the original configuration, but rather that there may be a number of "wild-type" configurations. It should be possible to distinguish some of these by differences in mutability. This would be, to me, a somewhat more satisfactory interpretation of

a delayed effect of a radiation than one where the absorbed energy is somehow merely stored by a "non-genic" molecule.

It should be a very simple matter to determine the genetic identity of spontaneous, zero-point, and end-point mutants. However, it should be pointed out that in K-12 there are at least three different genes mutation of which leads to resistance to T1. They are however phenotypically distinguishable. There may be others which are not which would complicate the story. At any rate it should certainly be done.

I am enclosing a not very good photograph that you may be interested to see: merely the phenotypes of the 4 combinations of Lac +/- and V_1 r/s . From an cross heterozygous for these factors, all 4 types are obtained as you have of course heard.

Hoping that you will be able to drop in up here,

With best regards

Yours sincerely,

